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Lateral Meningocele Syndrome: Three New Patients and Review of the Literature

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One female and two male patients with multiple lateral meningoceles are presented. They do not have neurofibromatosis or Marfan syndrome and share findings with the two previously described patients with multiple lateral meningoceles. The original report by Lehman et al. [1977: J Pediatr 90:49–54] was titled "familial osteosclerosis," because osteosclerosis was present in the proposita and her mother; the patient described by Philip et al. [1995: Clin Dysmorphol 4:347–351] also had increased bone density of the skull base and the sutures. Thickened calvaria were present in one of our patients; two had a prominent metopic suture. Other shared findings include multiple lateral meningoceles, Wormian bones, malar hypoplasia, downslanted palpebral fissures, a high narrow palate, and cryptorchidism in males. In addition, our patients showed ligamentous laxity, keloid formation, hypotonia, and developmental delay. A short umbilical cord was noted in two patients. One had a hypoplastic posterior arch of the atlas and an enlarged sella, as reported by Lehman et al. [1977]. Our patients appear to have the same syndrome as previously reported. We suggest it be called "lateral meningocele syndrome," because of this unique finding. Am. J. Med. Genet. 70:229-239, 1997.

KEY WORDS: atlas hypoplasia; connective tissue disorder; developmental delay; flattened mandibular angle; lateral meningoceles; malar hypoplasia; osteosclerosis; short umbilical cord

INTRODUCTION

Lateral meningoceles are protrusions of the arachnoid and the dura mater through inter- or intravertebral foramina. Although their development has not been studied, it seems likely that they occur secondary to dural dysplasia, such as dural ectasia. Dural ectasias arise from the pressure of the cerebrospinal fluid on a connective-tissue membrane that is weakened by a defect of extracellular matrix. They can present as widening of the neural canal, thinning of the bony cortex of the vertebral bodies and pedicles, dilation of neural foramina, or protrusion of dura outside the neural canal [Pyeritz et al., 1988]. Dural ectasias, including changes as severe as meningoceles, were found in 63% of patients with Marfan syndrome [Pyeritz et al., 1988]. Neurofibromatosis type I is seen in 63% of thoracic lateral meningoceles [Wilkins and Odom, 1978]; the underlying defect in this disorder may be bony, with vertebral scalloping, enlarged foramina, and deformed pedicles.

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An apparently unique syndrome with multiple lateral meningoceles was observed by Lehman et al. [1977] in a female with facial abnormalities and skeletal changes. The mother shared some of the facial and skeletal findings but did not have meningoceles. Philip et al. [1995] described a male with multiple lateral meningoceles and facial abnormalities. His skeletal changes were less severe than in the female, and in addition he had bilateral iris colobomata. He was thought to have the same syndrome as reported by Lehman et al. [1977].

Katz et al. [1978] described a 2-year-old male with multiple bilateral thoraco-lumbar meningoceles. The patient had failure to thrive, with normal OFC. He was described as having anomalies including epicanthal folds, low-set, and posteriorly angulated ears, micrognathia, and a flat nose. Unfortunately, no photographs were published and he is not available for reevaluation. In light of the anomalous findings, the multiple lateral meningoceles, and the absence of a family history and signs of neurofibromatosis or Marfan syndrome, it is possible that this patient also had the lateral meningocele syndrome.

We present three more patients with multiple lateral meningoceles and similar facial and skeletal abnormalities, who did not have neurofibromatosis or Marfan syndrome.

CLINICAL REPORTS

Patient 1

This Caucasian male was born at term after an uncomplicated pregnancy to a 30-year-old mother and a 33-year-old non-consanguineous father. He had one older, healthy brother. Vaginal delivery was complicated by placental abruption. He required supplemental oxygen postnatally but was not intubated. Apgar scores were 6 at 1 min and 8 at 5 min. A short umbilical cord was noted. Birthweight was 3.82 kg (90–95th centile), length was 52.2 cm (90th centile), and OFC was 33 cm (25th centile). Significant hypotonia was noted at birth and persisted, causing sleep hypoxia and requiring use of supplemental oxygen at night. A persistent ductus arteriosus (PDA) was closed at age 11 months by cardiac catheterization, and at that time a small muscular VSD, a retroesophageal, aberrantly arising right subclavian artery, and an interrupted inferior vena cava with azygous continuation were found. Bronchoscopy and esophagoscopy did not show compression secondary to the aberrant subclavian artery.

After the PDA repair a retrocardiac mass was seen on radiographs. On CT and MRI studies this mass was identified as one of multiple lateral meningoceles of the thoracic and lumbar spine (Fig. 1). The large size of the meningoceles caused partial atelectasis of the lungs and lateral displacement of the kidneys.

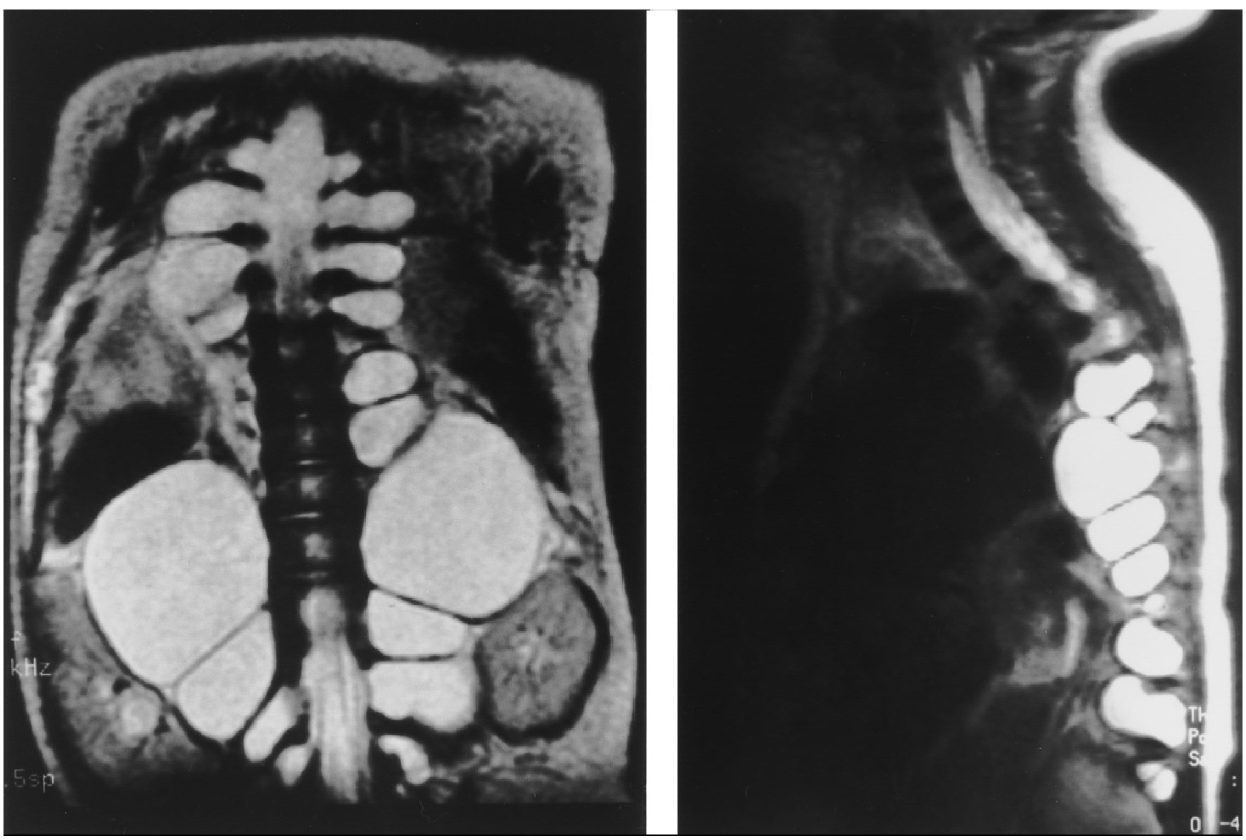

Fig. 1. Coronal and sagittal T2-weighted MR images of the thoraco-lumbar spine of patient 1 show multiple bilateral meningoceles, widening of the spinal canal, and enlarged neural foramina. Lumbar meningoceles displace the kidneys laterally.

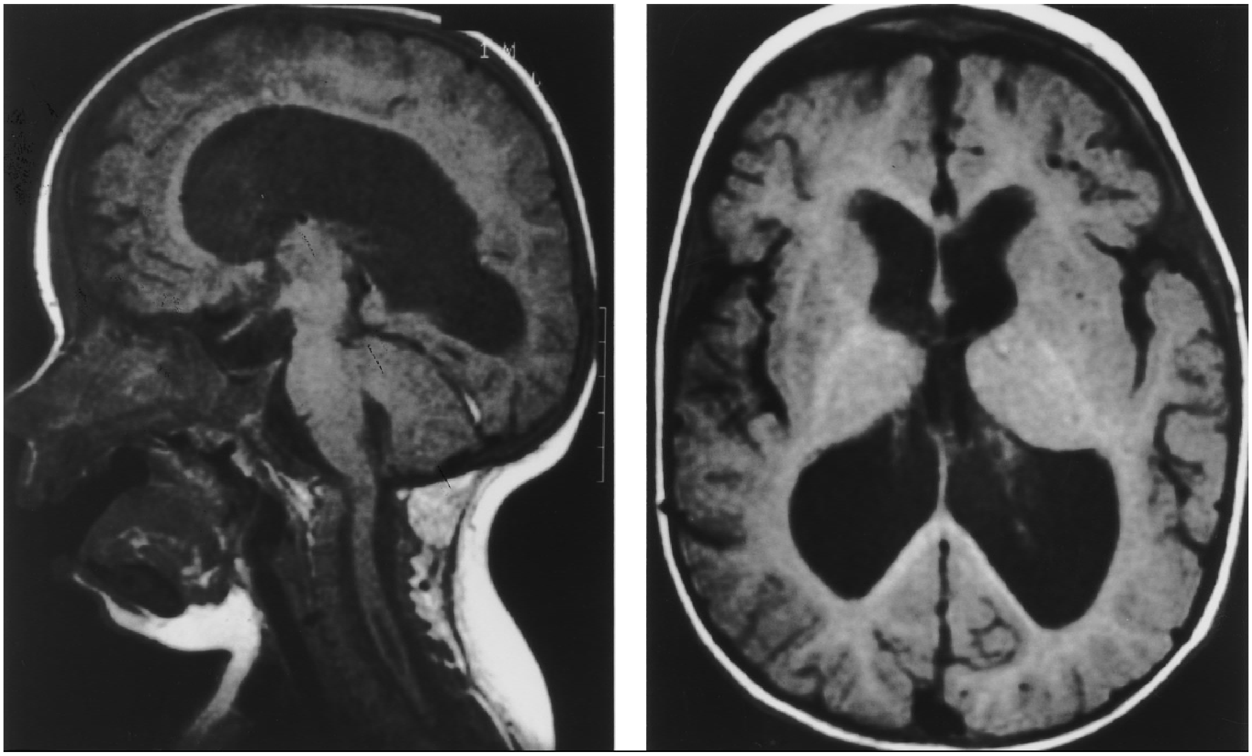

Fig. 2. Sagittal and axial T1-weighted MR images of the brain of patient 1 show ventriculomegaly, widened sulci and enlarged extra-axial subarachnoid spaces consistent with communicating hydrocephalus. A cervical syrinx is present. There is no empty sella.

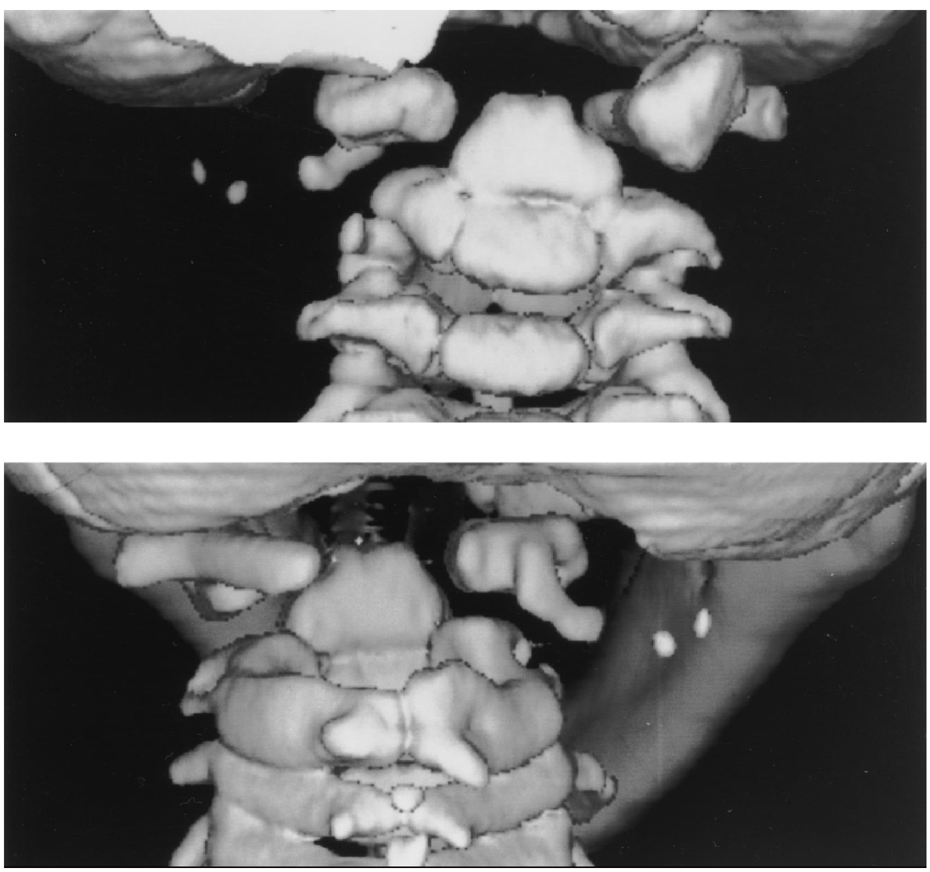

Fig. 3. Frontal (top) and posterior (bottom) view from three-dimensional helical computed tomography of the upper cervical spine of patient 1. The frontal view demonstrates malformed lateral masses of C1. The anterior arch is not visualized due either to aplasia or assimilation with the occiput. The posterior view of C1 shows hypoplasia on the left posterior arch and hemiaplasia on the right.

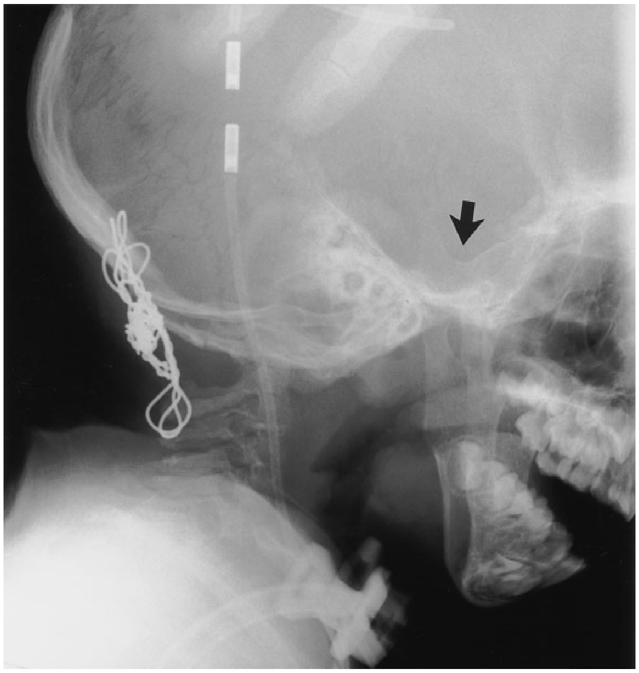

Fig. 4. Lateral radiograph of the cervical spine of patient 1, obtained after fusion of the occiput to C2, showing a diminished mandibular angle, a J-shaped sella (arrow) with a not unusually horizontal clivus, and multiple Wormian bones. The bones are mildly osteopenic. C1 is not clearly visualized.

Communicating hydrocephalus with wide subarachnoidal spaces, a Chiari I malformation and a small syringomyelia of the cervical cord were noted (Fig. 2). Because the hydrocephalus was thought to communicate with the meningoceles, a VP-shunt was placed at age 11 months in order to reduce volume and pressure in the meningoceles. After shunt placement the patient's motor development improved, he began to sit, and at age 16 months began to bear weight. Owing to progressive sleep apnea and swallowing problems a surgical decompression of the Chiari malformation was performed at age 22 months, along with a thoracic laminectomy and shunting of the largest thoracic meningocele to the pleura. During this procedure a malformed C1 vertebra was discovered. It consisted largely of a partially calcified excrescence of cartilaginous material, extending from the spinous process of C2 toward the foramen magnum (Fig. 3). The meningocele-pleural shunt caused significant pleural effusion and therefore was converted to a peritoneal shunt. Because of cervicomedullary instability, an occiput-C2 fusion with halo immobilization was performed at age 23 months. A tracheotomy was done at the same time because of persistent airway obstruction causing hypoventilation. An explorative laparotomy showed absent testes with vascular remnants bilaterally; these findings are indicative of prenatal testicular torsion leading to the "vanishing testes syndrome."

High resolution chromosome studies showed a 46,XY

Fig. 5. Patient 1 at 1 year; note flat supraorbital ridges, down-slanted lid axis and ptosis, broad nasal bridge, flat philtrum, micrognathia, apparently low-set and posteriorly angulated ears with prominent antihelices, low nuchal hair line, and short neck.

Fig. 6. Patient 1 at 2 years; note low nuchal hairline, hypertrichosis, soft tissue protrusions bilaterally in the lumbar area caused by meningoceles, and keloids over the iliac crests.

karyotype. Skull radiographs showed a diminished mandibular angle (160°, normal up to 130°), a large, flat sella and a moderate number of Wormian bones (Fig. 4).

At age 28 months length was 87.5 cm (10–25th centile) and OFC was 49.5 cm (50th centile). There was prominence of the metopic suture and flatness of the supraorbital ridges. The hair was coarse and curly with a very low nuchal hairline. There was a slight downslant of the lid axis, bilateral ptosis, and hypertelorism (interpupillary distance of 5.25 cm: 75–97th centile). The ears appeared low-set and posteriorly angulated with prominent antihelices. Malar hypoplasia, a flat and broad nasal bridge, broad anteverted nostrils, and a flat philtrum were seen (Fig. 5). The upper lip was tented and the palate extremely narrow and high-arched with wide gums. The upper middle incisors appeared large and micrognathia was present. The neck was short and webbed. There was mild pectus excavatum and normal spacing of the inverted nipples. A small umbilical hernia was seen. The genitalia were prepubertal, the penis appeared broad (5.5 cm long; 2 cm wide), testes were not palpable, and the scrotum was high positioned. Mild scoliosis was noted. Hypertrichosis was obvious on the back with a hair whorl in the midthoracic area. Bulging protrusions in the lumbar region bilaterally were caused by meningoceles (Fig. 6). Horizontal scars above the iliac crests, on the abdomen, and the occiput showed severe keloid formation, while vertical scars over the cervical and midthoracic spine and chest appeared well healed. Ligamentous laxity affected shoulders, elbows (20° hyperextension), MP joints, hips, knees (25° recurvatum), and ankles. No hyperextensibility of fingers or toes was noted. Generalized hypotonia without focal neurological abnormality was seen and muscle bulk appeared decreased. Owing to his ligamentous laxity the patient

Fig. 7. Patient 1 at 2 years, demonstrating extreme ligamentous laxity of the hips, tracheostomy, and abdominal keloid scar after peritoneal shunt placement.

tended to use his feet like his hands (Fig. 7). He walked with support and communicated through gestures.

Patient 2

This Caucasian male was born vaginally at term after an uncomplicated pregnancy to a 32-year-old primigravida. The mother had mitral valve prolapse and scoliosis. The 35-year-old father was in good health and there was no consanguinity. Apgar scores were 9 at 1 min and 10 at 5 min. Birthweight was 2.72 kg (10th centile), length was 52 cm (75–90th centile), and OFC was 32.5 cm(10–25th centile). The three-vessel umbilical cord was short (18 cm). Multiple congenital anomalies included receding forehead with prominent metopic suture, micro-retrognathia, apparently low-set and posteriorly angulated ears, redundant skin folds of the neck, and unilateral cryptorchidism. Generalized hypotonia was noted; developmental delay became obvious at age 8 months. He walked and spoke his first words at age 22 months. At age 7 years his IQ was 63 (Wechsler intelligence scale). Mildly delayed myelinization was noted on MRI of the brain at age 2 years; at age 6 1/2 years mild ventricular dilatation was seen. Bilateral ptosis, a right inguinal hernia with hydrocele, and cryptorchidism were surgically repaired.

Fig. 8. Radiograph of the spine of patient 2 shows thoracic kyphosis and widening of the neural foramina, especially in the lumbar region.

Fig. 9. A coronal T1-weighted MR image of the thoracic and upper lumbar spine of patient 2 shows multiple bilateral meningoceles with widening of the neural foramina and a capacious thecal sac indicating dural ectasia.

Radiographs of the spine were obtained at age 6 4/12 years because of a thoracic kyphosis of 75° and showed a lumbar spina bifida occulta and widening of the interpedicular distances (Fig. 8). An MRI scan showed multiple bilateral paraspinal meningoceles of the thoracic and upper lumbar spine (Fig. 9), and a small syringomyelia at the T8 level. The syrinx and the meningoceles remained unchanged in size and number on studies at age 8 years (Fig. 10). Marked scalloping of the posterior lumbar vertebrae and a capacious thecal sac indicating dural ectasia were noted. The kyphosis was treated by bracing, but worsened continuously and combined anterior-posterior spinal fusion from T1 to L3 was performed at age 8 11/12 years. During this procedure the largest visible thoracic meningocele, measuring approximately 6 cm in diameter, was incised. The spinal fluid pressure in the meningocele was 25–26 cm of water, fluctuating with breaths. Erosion of the vertebral pedicles above and below the meningocele was obvious. The spinal cord was visualized through an opening at the base of the meningocele into the spinal canal. The nerve roots passing through this meningocele appeared small, while the spinal cord appeared to be of normal size.

Skull radiographs performed at age 6 8/12 years showed diffusely thickened bone around the calvarium except for the occipital bone and thickening of the inner table with widened diploic space (Fig. 11). Multiple Wormian bones and an inca bone were noted. The sphe-

Fig. 10. T2-weighted sagittal MR image of the thoracic and lumbar spine of patient 2, showing lateral meningoceles with widening of the neural foramina and scalloping of the posterior surface of the vertebral bodies.

noid wings appeared abnormally ossified, with possible underdevelopment of the greater wings bilaterally. An enlarged aortic root measuring 2.39 cm (upper limit of normal 2.3 cm) was found on echocardiogram.

Studies with normal results included high resolution chromosomes, fragile X analysis, tests for prenatal infection, plasma amino acid and urine organic acid quantitation, serum copper and ceruloplasmin levels, screening for type I and type III procollagen and collagen synthesis and secretion, and radiographs of the hands; a soft tissue Technetium scan showed no neurofibromata in the thoracic and abdominal cavities [Mandell et al., 1989].

At age 8 years height was 125 cm (50th centile), span was 128 cm, weight was 24 kg (25-50th centile), and OFC was 55 cm (97th centile). Mild frontal bossing and

Fig. 11. Lateral radiograph of the skull of patient 2 shows thickening of the calvarium with a widened diploic space. Multiple Wormian bones are present. Sella and clivus are normal.

Fig. 12. Patient 2 at 8 years; note bilateral ptosis, down-slant of the lid axis and the long and smooth philtrum. Hair is coarse and straight, except for the temporo-parietal area.

prominence of the metopic suture were present. Hair was abundant, straight, and coarse, but in the temporo-parietal area it was in complete disarray, and there was a low nuchal hair line. The face was long and narrow and showed marked malar hypoplasia, residual bilateral ptosis, mild proptosis and a slight downslant of the lid axis (Fig. 12). Interpupillary distance was 5 cm (25th centile). The nose had a narrow root and a high narrow spine. The philtrum was long and smooth, the upper lip was thin and the chin had a square configuration. A high and narrow palate and severe dental crowding were seen. Ears appeared low-set and posteriorly angulated, with prominent antihelices and decreased cartilage resilience (Fig. 13). Increased AP diameter of the chest was caused by the kyphosis; a mild pectus carinatum was present. Areolae were normal in size and position. Cardiac and abdominal examination were normal. Genitalia were Tanner stage I, the penis appeared large (5.5 cm by 2 cm) and testes were descended. The skin was soft and mildly stretchable, without pigmentary changes. A keloid scar from a skin biopsy was present. Dermatoglyphics and palmar flexion creases were unremarkable. The extremities were straight and symmetric, with little subcutaneous fat (Fig. 14). Exaggerated lumbar lordosis and marked thoracic kyphosis without scoliosis were seen (Fig. 15). Ligamentous laxity was obvious with cubitus recurvatum of about 30° bilaterally, genu recurvatum of 25–30° bilaterally, and subluxable patellae and acromioclavicular joints. The fingers were extremely hyperextensible, long and cylindrical. The palms measured 8.9

Fig. 13. Patient 2 at 8 years, showing high nasal bridge, apparently low-set, posteriorly angulated ears with prominent antihelix, slight micrognathia and low posterior hairline.

Fig. 14. Patient 2 at 8 years, note slender built with little subcutaneous fat at the extremities, long fingers.

cm (75–97th centile) bilaterally and the third fingers 6.5 cm (75–97th centile). Muscle bulk and strength were normal. Generalized hypotonia without focal neurologic abnormality was noted.

Patient 3

This female was born at term after a pregnancy complicated by bilateral ovarian cysts and maternal cigarette use. Her 21-year-old primigravida mother and 31-year-old father were second cousins. Birthweight was 2.55 kg (10th centile). At age 7 months, gross motor developmental delay, hypotonia, and anomalies (hypertelorism, high palate, and micrognathia) were noted. She had recurrent urinary tract infections and failure to thrive. At age 14 months her weight was below the 3rd centile, length was at the 25th, and OFC was at the

Fig. 15. Patient 2 at 8 years, showing marked thoracic kyphosis and exaggerated lumbar lordosis.

20th centile. At that time she was able to pull to stand, but did not walk and was described as being irritable. Physical examination was remarkable for hypertelorism, downslanting lid axis, and bilateral ptosis. There was mild malar hypoplasia, apparently low-set and posteriorly angulated ears, a short webbed neck, and pectus excavatum. A mass was palpated in the right lower abdominal quadrant. No pigmentary skin changes were noted. She was hypotonic and had decreased muscle bulk.

Medial displacement of both kidneys and ureters was seen on an intravenous pyelogram. On abdominal CT scan large paralumbar cysts were noted. CT metrizamide myelogram showed multiple lateral meningoceles of varying sizes, located bilaterally from T8-9 to L5, and causing the renal displacement (Fig. 16). The meningoceles at the L5 level extended into the pelvis. Spinal radiographs showed posterior scalloping of T11–T12 and the lumbar vertebrae with marked thinning of pedicles and laminas. Because of the large intra-abdominal masses a lumbo-peritoneal shunt was placed. The patient's irritability improved after the procedure. A subsequent CT scan showed a considerable decrease in the size of the meningoceles. A CT scan of the brain was reportedly normal, as were chromosomal studies, an ophthalmological examination and an echocardiogram. The patient was thought to have Noonan-Neurofibromatosis syndrome [Hughes et al., 1986]. The diagnosis of Noonan syndrome was based on the facial characteristics and the short, webbed neck; neurofibromatosis was suspected due to its association with lateral meningoceles, but there were no signs of neurofibromatosis by age 9 years. The only newly reported finding at that time was a narrow maxillary arch.

DISCUSSION

Our patients share many abnormalities with those described by Lehman et al. [1977] and Philip et al. [1995] (Table I). All have multiple lateral meningoceles, and although thickened calvaria and a prominent metopic suture were noted in some, generalized osteosclerosis was not seen. In addition to the previously recognized characteristics of this syndrome [Philip et al., 1995], our patients had findings consistent with a connective tissue disorder, such as ligamentous laxity, keloid formation, and pectus malformation. While developmental delay and generalized hypotonia were noted in our patients, these findings were not noted in the previously described patients. Our patients appear to have the same syndrome as those two previously reported, and we suggest it be called "lateral meningocele syndrome," because of this unique finding.

Additional abnormalities may be part of this syndrome (Table I). Short umbilical cords were found in two of our patients. Findings commonly associated with a short umbilical cord include fetal hypokinesia, severe abdominal body wall defects, and monozygotic twinning [Blackburn and Cooley, 1993], none of which were present in our cases.

Abnormalities occurring only in patient 1 were PDA, VSD, an aberrantly arising right subclavian artery and interrupted inferior vena cava, a small umbilical hernia, and hypertrichosis. It is unclear if these and other findings seen in only one patient, like the iris colobomata in the case reported by Philip et al. [1995], are coincidental or if they are associated with the lateral meningocele syndrome.

A hypoplastic posterior arch of the atlas was present in our patient 1 and was described in the patient reported by Lehman et al. [1977]. It seems likely that a hypoplastic or partially aplastic posterior arch is part of the meningocele syndrome and should be investigated in patients with the syndrome, as it can lead to instability of the cranio-cervical junction. A posterior arch anomaly of the atlas was seen in two patients with Shprintzen-Goldberg syndrome [Sugarman and Vogel, 1982; Adès et al., 1995].

Similarities between our patients 1 and 2 and Shprintzen-Goldberg syndrome [Sood et al., 1996] in-

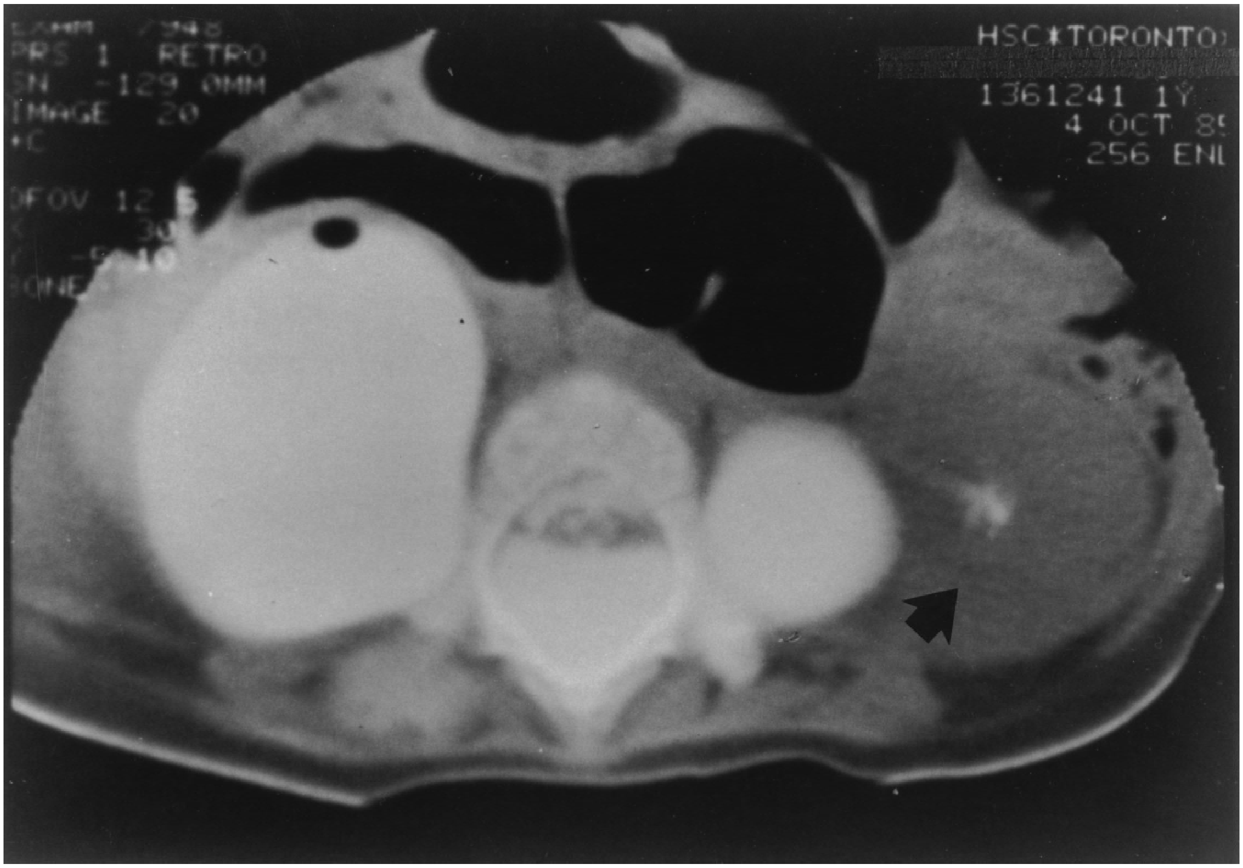

Fig. 16. Axial image from a CT myelogram of patient 3 showing an enlarged thecal sac and bilateral meningoceles, causing the displacement of the left kidney (arrow). Enlargement of the spinal canal is associated with scalloping of the vertebral body and thinning of the lamina and pedicles. Ectatic dural sleeves are seen along dorsal nerves entering the posterior spinal muscles.

clude proptosis, ptosis and downslanting palpebral fissures, maxillary hypoplasia, high arched palate, micrognathia, scoliosis, hypotonia, developmental delay, and, in patient 2, arachnodactyly and enlarged aortic root. Other findings characteristic for Shprintzen-Goldberg syndrome, such as craniostenosis, are absent in our patients, and lateral meningoceles have not been described in this syndrome.

Marfan syndrome, having dural ectasias and ligamentous laxity, shares some findings with the lateral meningocele syndrome. In two patients with Shprintzen-Goldberg syndrome a mutation in the fibrillin gene has been found [Sood et al., 1996], and the possibility of a genotypic continuum of this syndrome with the Marfan syndrome has been raised. There may be a continuum of the abnormalities in the fibrillin gene causing Marfan, Shprintzen-Goldberg and the lateral meningocele syndrome, which would be expected to show autosomal dominant inheritance.

An autosomal dominant inheritance pattern has been suggested for the lateral meningocele syndrome because of an affected parent and child [Lehman et al., 1977] and advanced paternal age in the second case [Philip et al., 1995]. The parents of our patients did not show the facial findings of the syndrome and none had a medical history indicative of neurological abnormalities. Radiographic examinations of the parents were not performed. If the inheritance pattern is indeed autosomal dominant, new mutations could have occurred in our patients, or the phenotype in the affected parent can be so mild that it cannot be detected without radiological studies. If the lateral meningocele syndrome is caused by a fibrillin gene mutation, the mitral valve prolapse and scoliosis seen in the mother of patient 2 may be indicative of a similar mutation in the mother. The consanguinity between the parents of patient 3, who are second cousins, also raises the possibility of autosomal recessive inheritance.

In summary, we suggest that the patients reported here have the same syndrome as those described by Lehman et al. [1977] and Philip et al. [1995]. Multiple lateral meningoceles in the absence of neurofibromatosis and Marfan syndrome are the most characteristic finding, thus we suggest naming it "lateral meningocele syndrome." Two patients had a hypoplastic posterior arch of the atlas, and since this can lead to instability of the cranio-cervical junction, patients with the lateral meningocele syndrome should be evaluated for this abnormality. In addition to the skeletal and facial abnormalities, a short umbilical cord, ligamentous laxity, cryptorchidism, keloid formation, hypotonia, and developmental delay were seen in some of the patients. The frequency of these findings in the lateral menin-

TABLE I. Findings in the Lateral Meningocele Syndrome

Findings	Patient 1	Patient 2	Patient 3	Lehman et al. [1977]	Philip et al. [1995]
Face					
Malar hypoplasia	+	+	+	+	+
Hypertelorism[a]	+	–	+	?	–
Downslanting lid axis	+	+	+	+	+
Ptosis[a]	+	+	+	?	+
Proptosis	+	+	?	+	+
High arched palate[a]	+	+	+	+	+
Apparently low-set, posteriorly angulated ears[a]	+	+	+	?	+ On photograph
Micrognathia	+	Mild	+	+	+
Skull					
Prominent metopic suture[a]	+	+	?	?	?
Thickened calvaria	–	+	?	+	Sclerosis of sutures; skull base
Wormian bones	+	+	?	+	+
Enlarged sella[a]	+	–	?	+	–
Flattened mandibular angle[a]	+	–	?	+	–
Skeletal					
Hypoplastic C1[a]	+	–	–	+	–
Short/webbed neck[a]	+	–	+	?	–
Pectus[a]	Excavatum	Carinatum	Excavatum	–	–
Scoliosis	+	+ kyphosis	–	+	+
Connective tissue					
Multiple lateral meningoceles	+	+	+	+	+
Keloid formation[a]	+	+	?	?	?
Inguinal hernia		+	–	–	–
Cryptorchidism[a]	+	+	N/A	N/A	+
CNS					
Chiari I malformation[a]	+	–	?	–	–
Hypotonia[a]	+	+	+	–	–
Developmental delay[a]	Mild	+	Mild	–	–
Other	Short umbilical cord, congenital cardiovascular abnormalities	Short umbilical cord, enlarged aortic root			Bilateral iris colobomata

[a]Denotes newly recognized characteristics.

gocele syndrome will become clear only after more affected individuals have been evaluated.

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